Indiana State Department of Health
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Michael R. Pence
Governor

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State Health Commissioner

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Dear Health Care Provider:

The following are the Indiana State Department of Health (ISDH) guidelines for evaluating and treating individuals exposed to a case of active TB Disease associated with a pan-sensitive TB isolate.

The Clark County and Floyd County Health Departments are conducting a contact investigation in which children and others who were possibly exposed to an index case are being screened for TB using PPD in a Tuberculin Skin Test (TST). A reading of ≥ 5mm of induration at 48-72 hours after TST placement or a positive blood interferon gamma release assay (IGRA) test is considered a positive result for both children and adults who are contacts of an active case. Most of those with a positive TST have been sent for x-rays. Individuals with a positive TST **MUST** be medically evaluated for symptoms of TB disease and abnormalities on chest x-ray to rule out active TB disease before being started on treatment for latent TB infection.

TB Disease (i.e. active or suspect tuberculosis)
Clinical Manifestations of TB Disease most often appear 1-6 months after infection in individuals who have not received treatment for latent TB infection.
Symptoms of Active TB Disease include fever, weight loss, or poor weight gain, cough, night sweats and chills.

Chest Radiography Findings after Infection are often abnormal in individuals with active TB disease. Common abnormalities include: lymphadenopathy of the hilar, subcarinal, paratracheal or mediastinal nodes; segmental or lobar atelectasis or infiltrate; pleural effusion; cavitary lesions; or miliary disease. A CT scan may be considered to characterize equivocal findings on CXR.

Laboratory Evaluation of a Patient Diagnosed with Active or Suspect TB Disease includes sputum collection for AFB smear and culture. Three specimens, preferably morning collections on three separate days, are needed. If the individual is coughing but cannot produce sputum consider saline induction of sputum. Clark Memorial Hospital can provide sputum inductions on an outpatient basis. There will be available slots on Monday – Thursday at 6 a.m. To schedule an induction, call 812-283-2405 and select option #2. Your office and the patient will be contacted prior to the induction to obtain all needed information. In some instances, it may be necessary to refer the individual for bronchoscopy in order to collect sputum for laboratory evaluation.

Treatment of TB Disease should be initiated immediately upon diagnosis. Individuals should be started on the four following antibiotics recommended for the treatment of pan-sensitive TB: isoniazid (INH), rifampin (RIF), pyrazinamide (PZA), and ethambutol (EMB). These

medications must be administered daily using directly observed therapy (DOT). Report the individual with a clinical diagnosis of TB disease to the local health department and the local health department will make arrangements with the individual for the directly observed therapy. DOT is the medical standard of care for TB disease and suspect cases of TB disease in Indiana. Drugs used for ongoing treatment of TB disease will depend on the sensitivity of the TB organism determined by results of the sputum culture.

Supplementation with 10-25 mg/d of pyridoxine (vitamin B6) is often prescribed with INH treatment of LTBI or TB disease to decrease the risk of drug-related peripheral neuropathy. It is specifically recommended for pregnant or nursing women and for breastfed infants. Pyridoxine is also recommended in the presence of other conditions associated with neuropathy such as diabetes, HIV, renal failure, and alcoholism. Pyridoxine supplementation is not felt to be required in individuals who are not in these categories due to adequate pyridoxine in there normal dietary intake.

The state of Indiana will provide appropriate medications for any individual with a suspect or confirmed diagnosis of TB disease, including pyridoxine. These drugs may be ordered through Purdue Pharmacy by e-script or calling 888-850-0037. Purdue pharmacists can also be consulted about dosing questions.

Latent TB Infection (quiescent TB infection without associated clinical signs or symptoms)

Latent TB Infection (LTBI) is diagnosed by the following:

- A TST≥ 5 mm induration in a person exposed to a person with infectious TB disease (considered a positive test) or a positive blood interferon gamma release assay (IGRA) test (e.g. T-Spot or Quantiferon-Gold test)
- No clinical symptoms upon medical assessment
- Normal chest x-ray

Treatment of Individuals with LTBI should be started on therapy *after ruling out active TB Disease*. Options for treating individuals with LTBI are provided in the table below and include:

- Isoniazid (INH) daily for 9 months
- Rifampin (RIF) daily for 4 months
- INH and Rifapentine once a week for 12 weeks. (This treatment regimen must be done by directly observed therapy. Please contact the local health department prior to initiating therapy to arrange direct observation of medication administration).

<u>The ISDH preferred regimen, when clinically appropriate, is the treatment protocol using isoniazid and rifapentine directly observed therapy once weekly for 12 weeks based on treatment efficacy and the increased likelihood of treatment completion</u>. This recommendation is based on expert opinion from the CDC and also three randomized controlled trials have shown that the new combination regimen of isoniazid (INH) and rifapentine (RPT) administered weekly for 12 weeks as directly observed therapy (DOT) is as effective for preventing TB as other regimens and is more likely to be completed than the U.S. standard regimen of 9 months of INH daily without DOT. In addition, the largest trial suggests higher efficacy in prevention of TB disease. The discontinuation of treatment and incidence of severe liver toxicity was less with INH/Rifapentine treatment group (see NEJM reference below). People started on mono therapy of either isoniazid or rifampin can be safely switched to the isoniazid/rifapentine regimen. Doses of mono-therapy

will not count toward completion of LTBI treatment. The patient must complete the 12 dose isoniazid/rifapentine regimen.

The Indiana State Department of Health will provide TB drugs free of charge through local health departments. However scripts need to be e-scripted or called to the Purdue Pharmacy in West Lafayette at 1-888-850-0037. Purdue pharmacists can also be consulted about dosing questions.

Also the chest x-ray results need to be faxed to the Clark County Health Department 812-288-1474 at the time drugs are ordered.

Routine determination of serum transaminase concentrations during the 9 months of therapy for LTBI is not indicated except for children and adolescents who: (1) have concurrent or recent liver or biliary disease; (2) are pregnant or in the first 12 weeks post-partum; (3) are having clinical evidence of hepatotoxic effects; or (4) concurrently are taking other hepatotoxic drugs (eg, anticonvulsant or HIV agents). If therapy is completed successfully, there is no need to perform additional tests or chest radiographs unless a new exposure to tuberculosis is documented or the child develops a clinical illness consistent with tuberculosis (2015 Red Book). For more detailed guidance, please consult the CDC document located at
http://www.cdc.gov/tb/publications/ltbi/treatment.htm

To speak with someone on the ISDH Provider Hotline call 844-257-0052.

Patient information sheet for INH/Rifapentine
http://www.cdc.gov/tb/publications/pdf/3hp_508.pdf
Patient information sheet for INH
http://www.cdc.gov/tb/publications/pdf/inh_508.pdf
Patient information sheet for RIF
http://www.cdc.gov/tb/publications/pdf/rif_508.pdf
Patient and general public materials
http://www.cdc.gov/tb/education/patient_edmaterials.htm

Choosing the Most Effective LTBI Treatment Regimen

http://www.cdc.gov/tb/publications/ltbi/treatment.htm#1

Drug(s)	Duration	Dose	Frequency	Total Doses
Isoniazid (INH)	9 months	Adult: 5 mg/kg Children: 10-20 mg/kg** Maximum dose: 300 mg	Daily	270
	6 months	Adult: 5 mg/kg Children: Not recommended Maximum dose: 300 mg	Daily	180
Isoniazid	3 months	Adults and Children 12 and over:	Once weekly†	12

(INH) and Rifapentine (RPT)		**INH*:** 15 mg/kg rounded up to the nearest 50 or 100 mg; 900 mg maximum **RPT*:** 10.0–14.0 kg 300 mg 14.1–25.0 kg 450 mg 25.1–32.0 kg 600 mg 32.1–49.9 kg 750 mg *≥50.0 kg 900 mg maximum*		
Rifampin (RIF)	4 months	Adult: 10 mg/kg*** Maximum dose: 600 mg	Daily	12 0

†Intermittent regimens must be provided via directly observed therapy (DOT), i.e., health care worker observes the ingestion of medication.
*Isoniazid (INH) is formulated as 100 mg and 300 mg tablets. Rifapentine (RPT) is formulated as 150 mg tablets in blister packs that should be kept sealed until usage.
** The American Academy of Pediatrics recommends an INH dosage of 10-15 mg/kg for the daily regimen and 20-30 mg/kg for the twice weekly regimen.
***In the United States, the recommended regimen for treatment of LTBI in children < 12 years of age is a 9-month course of INH. For the treatment of LTBI in infants, children, and adolescents when INH could not be tolerated or the child has had contact with a case patient infected with an isoniazid-resistant but rifamycin-susceptible organism the American Academy of Pediatrics recommends 6 months of daily rifampin (RIF) (180 doses) at a dosage of 10-20 mg/kg.

Information about using 12-week INH/Rifapentine therapy can be found at http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6048a3.htm?s_cid=mm6048a3_w

Sterling TR, Villarino ME, Borisov AS, et al. Three months of once-weekly rifapentine and isoniazid for M. tuberculosis infection. N Engl J Med 2011; 365:2155–66.